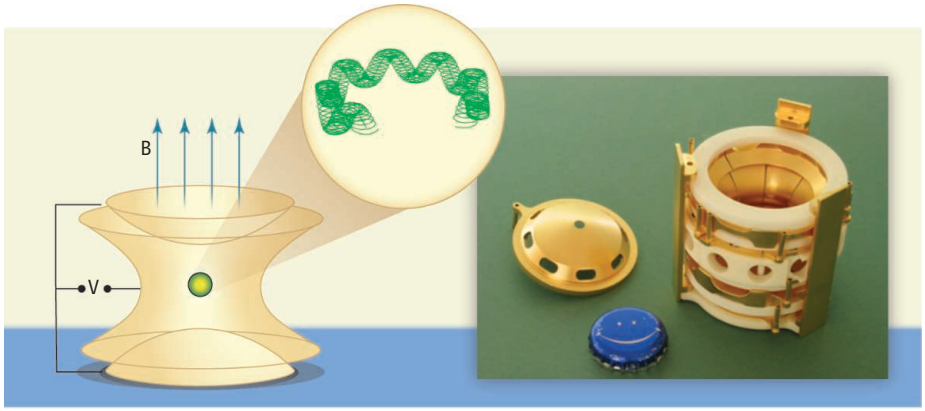
Microbial Cooperative Warfare

Hélène Morlon

Science **337**, 1184 (2012);
DOI: 10.1126/science.1227512

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005.



Trap and probe. (**Left**) Concept of a Penning trap and (**right**) example of a Penning trap configuration as used at LEBIT (*9*). With such electrode configurations, an ion can be stored in a strong magnetic field under vacuum for a long time. The frequency of the circular, cyclotron, motion performed by a trapped ion is connected to its charge, mass, and the magnetic-field strength. By determining this frequency, it is possible to obtain the ion's mass. Minaya Ramirez *et al*. have used a similar device in SHIPTRAP (*10*) for their study of nuclear binding of the heaviest elements.

of isotopes produced and delivered at half the speed of light.

SHIPTRAP (*10*) at GSI in Germany is the only ion trap facility specifically designed for the study of the heaviest elements. SHIPTRAP is connected to GSI's velocity filter SHIP, one of the few instruments in the world for the synthesis of superheavy elements. After a first demonstration of mass measurements of the heaviest elements (*11*), the SHIPTRAP team has now studied long series of nobelium and lawrencium isotopes in the vicinity of neutron number 152, where theory predicts a subshell closure (that is, stability).

The experimental results of Minaya Ramirez *et al*. corroborate the existence of this localized region of enhanced binding due to shell effects above the doubly magic lead-208 and confirm 152 to be a magic neutron number. Together with the shell effect strength that is extracted from the differences of the measured masses, this serves as a critical test for theoretical models describing the nuclear properties of the heaviest elements. Determination of this number is decisive for better predicting the location and the strength of the shell closures in heavier and superheavy elements.

Measurements such as those reported by Minaya Ramirez *et al*. are extremely difficult and require extraordinary care and preparation given the very low production rates of these very heavy elements and the need for high accuracy. In addition to providing a very important result, SHIPTRAP has set a new record by demonstrating that direct mass measurements of radioactive isotopes can be performed with detection rates as low as one ion every few hours while reaching an accuracy better than one part per million. The precise measurement of the mass of lawrencium-256 required the detection of about 50 ions and took 93 hours.

Extending such measurements to isotopes of even heavier elements is highly desirable and important but extraordinarily challenging; continued technical and methodological improvements will be needed. A new detection scheme is planned at SHIPTRAP where the mass of a single ion is measured by listening to the electric current it induces in electrodes due to its motion in the trap (*12*). Such single-ion sensitivity would be an important step in paving the way to the superheavy elements, in particular rutherfordium (proton number 104) and dubnium (proton number 105). If SHIPTRAP succeeds in measuring isotope masses of these elements, then it would help to unambiguously identify the new elements with proton numbers 113, 115, and 117 (*3*) by providing reliable mass anchor points for the alpha decay chains originating from these elements.

References

1. S. Hofmann, G. Münzenberg, *Rev. Mod. Phys.* **72**, 733 (2000).
2. K. Morita *et al*., *J. Phys. Soc. Jpn.* **73**, 2593 (2004).
3. Y. Oganessian, *J. Phys. G* **34**, R165 (2007).
4. L. Stavsetra *et al*., *Phys. Rev. Lett.* **103**, 132502 (2009).
5. D. Clery, *Science* **333**, 1377 (2011).
6. E. Minaya Ramirez *et al*., *Science* **337**, 1207 (2012); 10.1126/science.1225636.
7. K. Blaum, *Phys. Rep.* **425**, 1 (2006).
8. M. Mukherjee *et al*., *Eur. Phys. J. A* **35**, 1 (2008).
9. G. Bollen *et al*., *Phys. Rev. Lett.* **96**, 152501 (2006).
10. M. Block *et al*., *Eur. Phys. J. D* **45**, 39 (2007).
11. M. Block *et al*., *Nature* **463**, 785 (2010).
12. R. Ferrer *et al*., *Eur. Phys. J. Spec. Top.* **150**, 347 (2007).

10.1126/science.1228467

MICROBIOLOGY

Microbial Cooperative Warfare

Hélène Morlon

Analysis of microbial interactions in the wild shows that microbes cooperate to resist competition.

Cooperation among individuals of the same population directed against competing populations (cooperative warfare) is widespread in animals and plants. What happens in the microbial world is much less understood. Microbes can interact with one another through chemical signals, but little is known about the nature of their interactions, particularly outside the laboratory. On page 1228 of this issue, Cordero *et al*. (*1*) present a detailed analysis of ecological interaction networks, population structures, and genetic relatedness of microbes in the wild. They suggest that cooperative warfare is common in the microbial world.

To defend against invasion or invade established communities, microbes use a myriad of antibiotics. The interactions between producing (P), resistant (R), and sensitive (S) strains are often similar to the children's game "rock-scissors-paper," whereby P dominates S, S outcompetes R, and R outcompetes P (see the figure, panel A) (*2*). These strains cannot coexist in well-mixed populations (panel B). In spatially structured populations, they continuously displace one another, resulting in a dynamic mosaic of nearly clonal populations (panel C). Both theory and experiments suggest that such interactions promote coexistence and biodiversity (*2*–*4*). However, the extent to which they promote biodiversity in nature remains unclear.

To explore chemical warfare in the wild, Cordero *et al*. analyzed interactions within and between populations of bacteria of the family Vibrionaceae in the coastal ocean. The authors had previously identified ecological populations of *Vibrio* on the basis of

Center for Applied Mathematics, UMR 7641 CNRS, Ecole Polytechnique, Route de Saclay Palaiseau, 91128 France. E-mail: helene.morlon@cmap.polytechnique.fr

a protein-coding gene phylogeny and habitat associations (*5*). In the present study, they systematically analyzed pairwise interactions among 185 *Vibrio* isolates by means of local growth inhibition tests.

They identify a certain degree of genetic difference above which the potential for antagonistic interactions increases sharply. This threshold coincides almost exactly with the average genetic distance separating ecological populations. Hence, antagonism occurs mostly between rather than within natural *Vibrio* populations. Moreover, whole-genome analyses reveal that genomes of the same population share on average only 72% of their genes. Thus, populations are not nearly clonal, contrary to what would be expected under cyclic replacement [(*2*), panel C]. Rather, coexistence is maintained by a cooperative population structure (panel D).

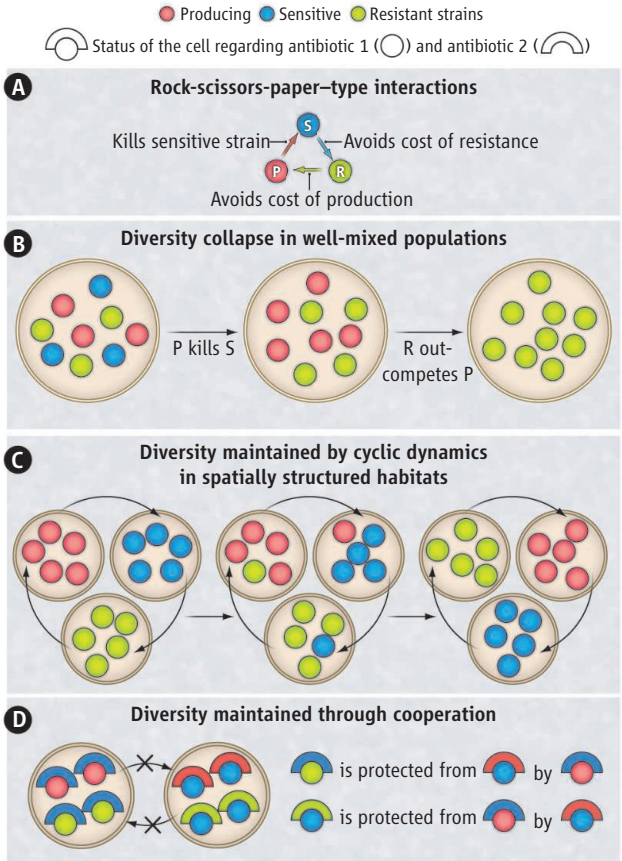
The idea that microorganisms can participate in social behaviors similar to those of macroorganisms is not new (*6*, *7*). Microorganisms cooperate to better exploit resources (*8*), to form microbial mats or fruiting bodies (*6*), and to resist stressful environments (*9*). Cordero *et al*. show that cooperation is also a major force in antibiotic-mediated interference competition between populations. Research on interference competition in microbes has focused on the role of proteins (*10*), but the authors show that most interactions (96%) are in fact mediated by small antibiotic molecules. A single specific antibiotic biosynthesis cluster, apparently subject to frequent horizontal transfer, seems responsible for the antagonistic activity.

Cordero *et al*.'s study suggests that in socially cohesive bacterial populations, superkiller strains release antibiotics that act as "public goods." But how can such social systems evolve? Antibiotic production comes at a fitness cost to the superkillers, and in a Darwinian world of survival of the fittest, why should an individual help others at its own expense? Hamilton's theory of kin selection stipulates that cooperation can be maintained in a population if the cooperative behavior is directed toward relatives carrying the cooperative genes (*11*). Antagonism decreases with genetic relatedness in *Vibrio* populations, which could suggest a form of kin selection. However, the authors found that the nonproducing cells toward which cooperation is directed do not carry genes from the antibiotic biosynthesis cluster.

This observation raises the intriguing possibility that cooperation can be maintained in microbial populations if it is directed not only toward cells carrying the cooperative genes, but also toward cells that have a greater potential to acquire these genes. Indeed, the cells benefiting from cooperation are already resistant and can thus readily acquire antibiotic-producing genes by horizontal transfer. Nonresistant cells are much less likely to acquire these genes, because producing genes are not genetically linked to their resistance factors. Further empirical and theoretical work aimed at testing this hypothesis will advance our understanding of microbial social structure.

Cordero *et al*. have assembled one of the largest microbial interaction networks to date. A similar network was recently compiled for *Streptomyces* (*4*). Studies of this kind open promising avenues for analyzing ecological networks and will likely bring new insights into the evolutionary ecology of communities. However, the high-throughput growth methods used in these studies have shortcomings. Experiments carried out in a fixed culture medium might not capture what happens in nature, because interactions can vary drastically with environmental conditions (*12*). Likewise, cultivation-dependent techniques presumably miss many strains. It would be insightful to compare these networks to in silico networks constructed from genome-scale models (*12*), or to networks estimated from spatial and temporal associations among microbial taxa identified by molecular techniques (*13*).

Still, a property that seems to emerge across microbial networks is that interactions evolve quickly. This contrasts with the evolutionary conservatism of interactions generally observed in macroorganisms (*14*). Rapid evolutionary changes of ecological interactions imply that we face a daunting task of predicting the future effect of environmental changes or clinical treatments on microbial communities. Further exploration of the evolution of microbial interaction networks may prove crucial to meet major challenges ahead, including evaluating how the ecological services provided by microorganisms will respond to global change and designing effective treatments against resistant bacterial infections.



Diverse views of coexistence. (**A**) Antibiotic production often results in rock-scissors-paper–type interactions between bacterial strains. (**B**) In the absence of spatial structure, producing strains kill sensitive strains and resistant strains outcompete producing strains, resulting in diversity collapse. (**C**) In structured habitats, clonal populations are constantly invaded and replaced in a dynamic game, thus maintaining diversity. (**D**) Cordero *et al*.'s results suggest that in nature, cooperation within nonclonal populations prevents invasion and maintains diversity.

References and Notes

1. O. X. Cordero *et al*., *Science* **337**, 1228 (2012).
2. B. Kerr *et al*., *Nature* **418**, 171 (2002).
3. T. L. Czárán *et al*., *Proc. Natl. Acad. Sci. U.S.A.* **99**, 786 (2002).
4. K. Vetsigian *et al*., *PLoS Biol.* **9**, e1001184 (2011).
5. D. E. Hunt *et al*., *Science* **320**, 1081 (2008).
6. B. J. Crespi, *Trends Ecol. Evol.* **16**, 178 (2001).
7. S. A. West *et al*., *Nat. Rev. Microbiol.* **4**, 597 (2006).
8. A. S. Griffin *et al*., *Nature* **430**, 1024 (2004).
9. H. H. Lee *et al*., *Nature* **467**, 82 (2010).
10. M. A. Riley, J. E. Wertz, *Annu. Rev. Microbiol.* **56**, 117 (2002).
11. W. D. Hamilton, *J. Theor. Biol.* **7**, 1 (1964).
12. S. Freilich *et al*., *Nat. Commun.* **2**, 589 (2011).
13. J. A. Steele *et al*., *ISME J.* **5**, 1414 (2011).
14. J. M. Gómez *et al*., *Nature* **465**, 918 (2010).

Acknowledgments: I thank B. J. M. Bohannan, J. L. Green, S. Kefi, and J. B. Plotkin for comments on a previous draft. Funding was provided by the CNRS and ANR grant ECOEVO-BIO-CHEX2011.

10.1126/science.1227512